No significant gender difference in hospitalizations for acute coronary syndrome in Switzerland over the time period of 2001 to 2010

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Abstract

Background: Morbidity and mortality from cardiovascular diseases have decreased since the 1970s in most Western societies. However, it is unclear if this positive trend can also be found in younger women suffering from acute coronary syndrome (ACS).

Methods: This is a prospective single center registry study including 11.015 women and men hospitalized for a first ACS between the years 2001 and 2010. We analyzed ACS rates according to sex and age group using Poisson regression in order to assess temporal trends.

Results Overall ACS hospitalization rates per 100.000 inhabitants increased by 31% between 2001 and 2010 (Rate Ratio (RR) of 1.31, 95% CI 1.20–1.43; $p < 0.001$) with a similar increase in men (RR 1.29, $p< 0.00001$) and women (RR 1.35, $p<0.0001$). Analyses of age-specific ACS rates showed a significant increase in ACS hospitalization rates only for the age groups 70-79 years ($p = 0.003$) and 80+ years ($p < 0.00001$). None of the age matched subgroups showed a sex related significant difference in trend for ACS hospitalization rates. Temporal trends for recorded risk factors showed a significant increase in smoking ($p=0.03$), and a trend to increased obesity prevalence ($p=0.06$) in females in the age group 60-69 years.

Conclusions: In contrast to other studies, we found no evidence for a particular increase in the number of younger women referred for a first ACS during the years 2001 and 2010. Potential negative effects of smoking and obesity on ACS incidence may be delayed to women older than 70 years.

Keywords: acute coronary syndrome, gender, women, age, cardiovascular risk factors

Introduction

Cardiovascular diseases (CVD) and in particular coronary artery disease (CAD) remain the leading cause of morbidity and mortality for both women and men in industrialized countries [1,2], such as in Switzerland.[3] The incidence of acute coronary syndrome (ACS) is related to risk factor levels in the population.[4] Recent publications regarding ACS and CAD incidence from USA and Europe show fluctuations in rates before 2000[5-10] followed by a decline during the last decade[11-14], except for Spain, for which increased rates have been reported[15]. This generally declining trend is considered to be due to better identification and control of cardiovascular risk factors[9,10], to improved drug regimens for CAD and to enhanced myocardial revascularization strategies[5,7-10]. A majority of the studies state overall age-standardized rates, while data on age-specific trends are rare. Taking age and sex into account, increasing trends in ACS incidence have been reported among younger women compared to younger men[16-18]. Potential explanations comprise non-favorable trends in cardiovascular risk factors in adolescents and young adults and in non-atherosclerotic causes of the disease in younger age groups[19]. While most Western countries show a promising negative trend in smoking prevalence, overweight and type 2 diabetes are generally increasing[3,20-21].

The aim of this study is to investigate sex and age-specific trends in male and female patients with ACS using data from a tertiary care center with stable referral area in Switzerland taking into account age subgroups and to investigate underlying changes in risk factor profile during the time period of 2001 to 2010.

Methods

Study population

Over the time period of 2001-2010, the Cardiology Clinic of the University Hospital of Bern (Inselspital Bern) was serving a referral area of about 1 million people and was the biggest respective tertiary care center in Switzerland. During the study period, 53% of patients have been referred for ACS from the canton Bern (BE), 18% from den canton Solothurn (SO), approximately 10% from the canton Fribourg (FR) and the remaining from either canton Ticino (TI) or canton Neuchâtel (NE). Referral area remained stable throughout the inclusion period, except for the canton NE replacing the canton TI. Until 2001, canton TI referred 5.3% of all patients and then ceased referral, whereas in the year 2001 canton NE started to refer approximately the same proportion of patients. The number of competing institutions has not changed during the study period: whereas an additional clinic started offering coronary interventions in the year 2006, their influence on referral numbers was offset by the fact, that in the same year a clinic with a comparable catchment area started allocating their patients to the Bern University Hospital. Referrals from outside the predefined area were minimal (≤ 20 per year). Demographic data on the referral cantons was provided by the Swiss Federal Statistical Office (BE, SO, FR and NE from 2001-2010).

Immigration to Switzerland increased from 124'077 in 2001 (63'139 men and 60'938 women) to 181'778 in 2010 (85'265 men and 96'513 women), with a majority from the age group of 20-39 years and therefore low risk for ACS.

We included all patients with ACS undergoing coronary angiography and therefore fulfilling eligibility criteria for an invasive procedure. At our tertiary care center, coronary angiography is performed in all ACS patients without absolute contraindications for invasive procedures. University Hospital Bern has been using electronic data storage for all coronary angiography reports since the early 1990s, including basic demographic data, and this database was used for numerous publications over the last years[22-24] . Diagnoses were recorded as determined by the attending physicians based on clinical, electrocardiographic, and biochemical (elevated troponin levels) criteria. Definitions of type of myocardial infarction (ST-elevation vs non-ST-elevation) and unstable angina were homogeneous and based on criteria according to current guidelines[25]. Only first ACS events were included and patients with a history of ACS, data of angiographies conducted on a second or later event as well as all angiographies performed later than 2 weeks after initial diagnosis of ACS, were excluded. Furthermore, presence and extend of coronary artery disease have been recorded. For our study, a vessel was considered to be affected when a stenosis of ≥50% was present, which led to the definition of one, two or three vessel disease.

Cardiovascular risk factors

Arterial hypertension, dyslipidemia and diabetes mellitus were recorded if stated in the patient history or when the individual medication list at entry contained medication to control these risk factors prior to the index hospitalization. Smoking status and family history for CAD were also extracted from the patient history. Smoking was defined as current smoker or smoking cessation within one year prior to the ACS. Obesity was defined as body mass index >30 kg/m2.

Statistical analysis

For the statistical analyses, we grouped the patients according to age into 5 different age groups: 20-49 years, 50-59 years, 60-69 years, 70-79 years and 80-99 years. We calculated the annual number of first ACS by age groups for men and women, and, using the demographic data of the catchment area, calculated rates of ACS hospitalization per 100.000 population of each specific sex and age group. To assess temporal trends of the ACS hospitalization rates, we performed univariate and multivariate Poisson regression analyses. For these, the total number of ACS hospitalizations was considered to be Poisson distributed given the total population of the catchment area[26]. A p-value of ≤0.05 was considered statistically significant. All analyses were performed using Stata Version13.

Results

ACS hospitalizations

During the study period from 2001-2010, a total of 11.015 coronary angiographies were performed in patients hospitalized with a first ACS (69.9% men). With very few exceptions, patients have been Caucasian by race. Men were younger than women (62.3 ±12.3 vs. 69.2 ±11.5 years; $p < 0.001$). Over time, there was a significant increase in mean age at ACS onset for both sexes. Mean male age increased from 61.7 in 2001 to 63.6 in 2010, whereas mean female age increased from 67.8 in 2001 to 70.2 in 2010.

Overall ACS hospitalization rates per 100.000 inhabitants (Figure 1) increased by 31% between 2001 and 2010 (Rate Ratio (RR) of 1.31, 95% CI 1.20–1.43; $p < 0.001$) with a similar increase in men (RR 1.29, $p< 0.00001$) and women (RR 1.35, $p<0.0001$). No statistical difference in trends for ACS hospitalization rates could be observed between the sexes ($p=0.254$). Trends in ACS hospitalization rates over the study period were not significantly different after age-adjusted analysis for males and females.

Analyses of age-specific ACS rates (Figure 2) showed a non-significant increase in ACS hospitalization rates for the age groups 20-49 years ($p = 0.4558$), 50-59 years ($p = 0.5110$) and 60-69 years ($p = 0.6122$). We found a significant increase in ACS hospitalization rates for the age groups 70-79 years ($p = 0.003$) and 80+ years ($p < 0.00001$). Sex-specific analyses showed that ACS hospitalizations increased in the 70-79 years old men and in the 80+ years male and female population. None of the age matched subgroups showed a sex related significant difference in trend for ACS hospitalization rates.

Hospital mortality

Data on hospital mortality in ACS patients in our cardiology clinic are only available since the year 2008 and was 5.6% in 2008, 5.1% in 2009 and 4.4% in 2010. However, this data correspond well to data from the AMIS (Acute Myocardial Infarction in Switzerland) Registry[27] which included 21'620 STEMI-patients, 5786 women and 15'834 men from 78 Swiss hospitals over the time period between 1997 and 2011, where they found a decrease of in-hospital mortality from 10 to 5% in men and from 18 to 7% in women during this time period.

Cardiovascular risk factors
Temporal trends with regard to the risk factors obesity, diabetes and smoking are shown in Figure 3 according to different age groups and displayed separately for men and woman.

Obesity in ACS patients increased by 4% over the whole study period and was higher in females (Relative Proportion of (RP) 1.21, 95%-CI: 1.10-1.34) compared to men. 80+ years ACS patients were 37% less obese compared to the youngest age group (20-49 years). This trend is not significantly different from overall trends in cardiovascular risk factors in Switzerland over the time period[27.]

Severity of coronary artery disease
The number of affected vessels per patient (≥50% stenosis) remained stable in the younger age groups, whereas the proportion of patients with one vessel disease decreased significantly in the age groups 60-69 and 70-79 years (p=0.002), but without significant differences between sexes.

Discussion

We found a significant overall increase of ACS referral rates to a tertiary care center in men and women over the time period of 2001 to 2010 in an area of Northwestern Switzerland with approximately 1 million inhabitants. However, the main driver for this increase was the very elderly population. No significant differences in sex specific trends were observed. In particular, we found no significant increase of referrals of younger women for ACS during this time period.
Our findings are in contrast to several large studies[28-30] reporting an increase in the proportion of women presenting with ACS. However, others have shown a significant decline in the proportion of women presenting with ACS over the past decade[31]. A potential explanation for these discrepancies is a decrease in the rates of ST-elevation myocardial infarction (STEMI) in both men and women, in accordance with global trends combined with an increase in the diagnosis of non-ST-elevation myocardial infarction perhaps due to corresponding changes in the definition of acute myocardial infarction during (AMI) the last decade[25] and to the increased use of sensitive troponin serum assays during this time period.
Mean age of ACS onset increased significantly for both sexes. Women presenting with ACS

have consistently been shown to be older and to have more comorbidities when compared with men.[30-34] Furthermore, a registry study from Sweden reported an increase in the use of PCI during index hospitalization in recent years in women with ST-elevation myocardial infarction[35]. With regard to age group several studies have analyzed ACS hospitalization rates among young adults[18,36-38]. Many prior studies reported increasing hospitalization trends in a younger population and particularly in women. McManus et al.[39] found an increase in hospitalization rates of young individuals (<55 years) with STEMI during 1997–2005. Another study found an increase in ACS hospitalization rates among women 20–49 years during 1994–2004[36]. Similar increasing trends were reported by Towfighi et al.[38] for hospitalization rates among women 35–44 years during 1997–2006 and Nedkoff et al.[40]found an annual increase of 4% in ACS incidence rates in women aged 35–54 years in Western Australia during 1996–2007. We cannot confirm an increase in hospitalization for ACS patients less than 50 years of age among our study population. Only the increase in the oldest age group (80+) was significant and can be explained by the increasing practice of invasive procedures in the very elderly, parallel to the higher life expectancy. As shown in a large Italian cohort study consisting of 89.562 patients, the use of an invasive approach increased markedly over time in both sexes (from 54.9% in 2000 to 91.9% in 2010 in men; from 36.8% in 2000 to 72.0% in 2010 in women), while the change was mainly driven by the subgroup of patients aged 75+ years[41]. Similar in Switzerland, where the procedure of coronary angiography and PCI in ACS gained importance during the 1990s and rapidly replaced systemic thrombolysis. Improved safety and feasibility of coronary interventions during the past decade lead clinicians to include older and more fragile patients. In particular, the underrepresentation of the very elderly and other vulnerable groups such as renal patients[42] in a majority of clinical trials underpins the importance to adequately consider the changing age demographics and extension of established therapies to more borderline populations.

Over the recent years, most studies from the US and across Europe have shown decreasing rates of ACS but differing trends in ACS hospitalization[11,43] . In Scandinavia and in particular Norway and Sweden, ACS incidence rates declined during the first decade of the 21st century, with a more pronounced decline in men than women[44,45], and similar tendencies have been reported from the Netherlands during 1998–2007[14,46] and the UK during 2002-2010[47].

Compared to the general decrease in ACS for both sexes and across all age groups, hospitalizations for ACS have a more ambiguous pattern with widely differing trends among gender and age groups[48]. This overall decrease in ACS, in the face of partly stable or even increasing hospitalizations for ACS most likely mirrors the advances in preventive care. In particular, wide spread acceptance of evidence based preventive drug therapy leading to decreased ACS morbidity, combined with increasingly sensitive cardiac biomarker assays, continuous improvement in rapid response networks and ubiquitously implemented rapid reperfusion facilities, is ultimately leading to increased hospitalization rates but decreased mortality. However, because Switzerland has a highly developed health system with optimal prevention and treatment facilities of ACS very different from many other countries[49], the data are not easily generalizable. And immigration seems not to have a significant impact on hospitalization rates for ACS in our study cohort due to the relatively young age of most immigrants and very low ACS risk in this age group.

During the study period, no significant differences have been observed in the cardiovascular risk profile, except for the 60-69 years age group, in whom prevalence of smoking and obesity increased slightly (Figure 3). The prevalence of hypertension,

hypercholesterinemia and smoking has substantially decreased in recent decades in most populations. However, increasing prevalence of smoking (especially among young women), obesity and physical inactivity in subgroups of adolescents and young adults have been reported and may have contributed to unfavorable trends in ACS in several countries[9,10]. This is supported by a high prevalence of these risk factors observed among young adults hospitalized for their first AMI[28]. Within the WHO-MONICA study, it was estimated that trends in major risk factors, such as systolic blood pressure, smoking and serum cholesterol levels, explained 40% and 15% of the variability in coronary event rates in men and women, respectively. Despite the lack of regional data on trends in risk factors in the investigated referral area, national health surveys in Switzerland have shown an overall reduction in hypertension, and serum cholesterol levels, similar to those reported from other countries. However, - as an exception - smoking increased in younger women age 15-24 years, whereas obesity and physical inactivity increased in all age groups.

Limitations

Our dataset does not represent the total number of ACS which occurred in the reference area over time but rather hospitalization rates for ACS and therefore includes referral bias. However, we assume that over the time period 2001-2010 indication for referral of ACS cases to a tertiary care hospital did not change except for an expansion of indications for interventional procedures in very elderly people in the age range 80+ years. Furthermore, our data does not include information on ACS subtype, therefore we are not able to examine whether the trends observed apply to different ACS subtypes. Our investigation is restricted to hospitalized patients with ACS and angiography and does not include patients hospitalized with ACS but with absolute contraindications for angiography and pre-hospital ACS cases including out-of-hospital cardiac arrests. However, due to the large number of patients included, it is unlikely that the inclusion of these cases would have significantly influenced time trends over particular age groups and gender.

Strengths

Our study is the first to report gender specific trends in AMI incident hospitalization in a representative and stable referral area in Northwestern Switzerland, using data from a single tertiary care center registry. We included all individuals 20 years and older who were hospitalized for ACS during 2001–2010, whereas most previous studies have been limited in regard to the range of included age groups in particular by excluding the very elderly. Serum troponin use was adopted by the University Hospital of Bern during 1998–2000 and therefore we expect minimal preconception due changing diagnostic criteria.

Conclusion

Whereas overall hospitalization for first incident ACS in patients 20-100 years of age increased in Switzerland during 2001–2010, the single driver of this increase was found to be the age group of the very elderly (80+), with no differences in gender and age specific trends. This may be due to favorable trends with overall reduction of smoking, hypertension and serum cholesterol levels in our population. However, a significant increase in smoking prevalence and a trend towards increasing obesity in women in the age group 60-69 years may indicate that a negative impact of these risk factors on ACS incidence may be delayed to older age groups.

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Figure Legends

Figure 1: ACS rates (events/100'000 inhabitants) in men and women from 2001 to 2010

Figure 2: ACS hospitalization rates of men and women according to age groups from 2001 to 2010

Figure 3: Percentage of ACS patients presented with the risk factors obesity, diabetes or smoking from 2001 to 2010 (top: men; bottom: woman; left: 20-49 years; middle: 50-59 years; right: 60-69 years)

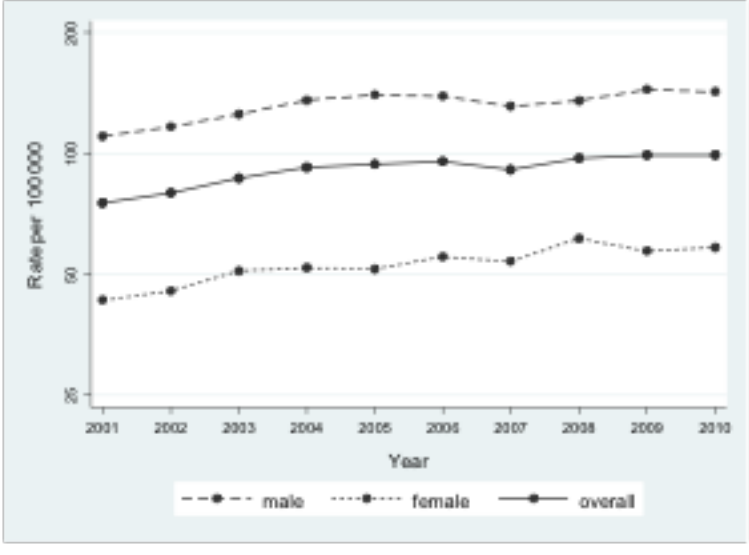

Figure 1

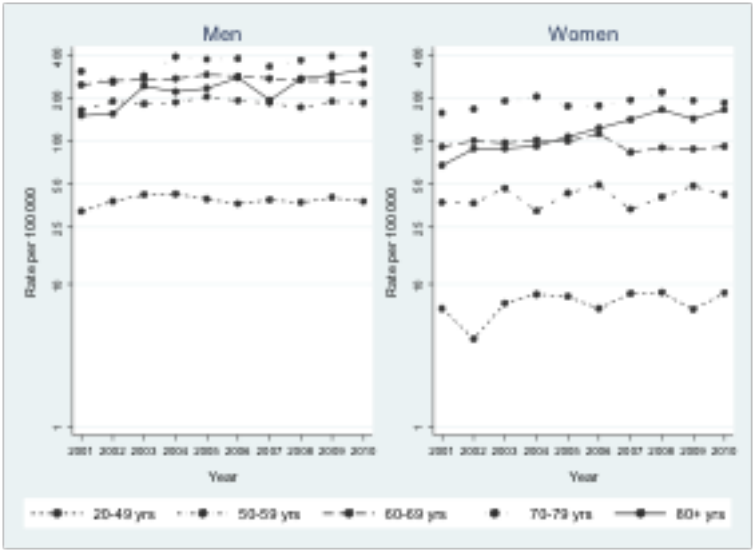
Men
Women
Rate per 100 000
Year
20-49 yrs
50-59 yrs
60-69 yrs
70-79 yrs
80+ yrs

Figure 2

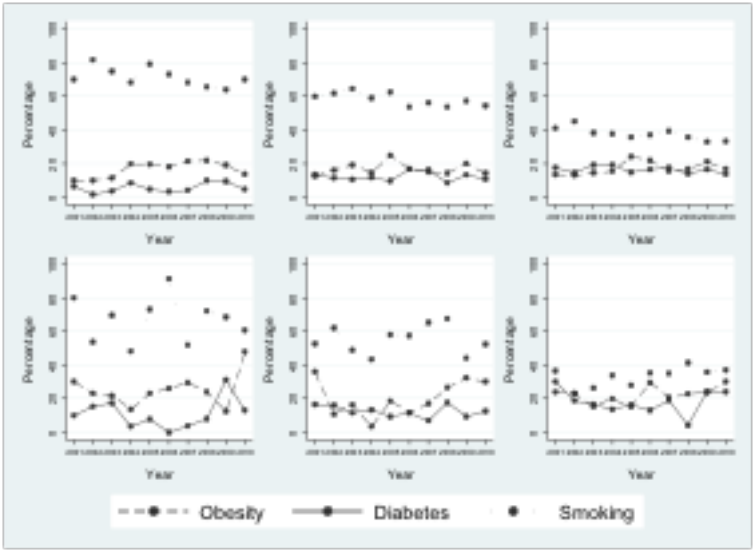

Figure 3